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A STUDY COMPARING THE EFFICACY OF PREMIXED VERSUS SEQUENTIAL ADMINISTRATION OF FENTANYL AND BUPIVACAINE IN SUBARACHNOID BLOCK FOR BELOW UMBILICAL SURGERIES

Anaesthesiology

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ABSTRACT

Background: In subarachnoid block numerous adjuvants like morphine, clonidine, midazolam, dexmedetomidine and fentanyl etc have been added with hyperbaric bupivacaine to increase the duration of sensory and motor block, to provide stable haemodynamics and prolonged postoperative analgesia for below umbilical surgeries. The aim of the present study was to evaluate the effect of premixed versus sequential administration of fentanyl and hyperbaric bupivacaine in subarachnoid block on block characteristics, haemodynamic parameters and postoperative analgesia. **Methods:** Ninety patients were randomly allocated into three groups of 30 each: Group A received premixed 0.5% heavy bupivacaine 2.5 ml (12.5 mg) and 0.5 ml (25 µg) of fentanyl in a single 5.0 ml syringe, Group B received 0.5 ml (25 µg) of fentanyl in a 2.0 ml syringe followed by 0.5% heavy bupivacaine 2.5 ml (12.5 mg) in a 5.0 ml syringe, Group C received 0.5% heavy bupivacaine 2.5 ml (12.5 mg) in a 5.0 ml syringe followed by 0.5 ml (25 µg) fentanyl in a 2.0 ml syringe. **Results:** The mean time for onset of sensory and motor block was least in group C followed by group B. The duration of sensory and motor block was prolonged in groups B and C. Patients in group A experienced more hypotension as compared to groups B and C. **Conclusion:** Administering hyperbaric bupivacaine first followed by fentanyl leads to an early onset and prolonged duration of sensory and motor block and haemodynamic stability.

KEYWORDS

Bupivacaine, Fentanyl, Motor Block, Premixed, Sensory Block, Sequential, Sub Arachnoid Block

INTRODUCTION

Regional anaesthesia is the preferred technique for below umbilical surgeries. It allows the patient to remain awake, minimize or completely avoid the problems associated with airway management. Subarachnoid block is one of the most versatile regional anaesthesia techniques used for below umbilical surgeries due to its low cost, simple technique, higher patient acceptance and lower incidence of major perioperative complications achieved by a limited and localised action of the drug.[1]

Choice of local anaesthetic (LA) utilized in subarachnoid block is based on the pharmacologic properties of the drug.[2] Bupivacaine an amide type of LA, has high potency, slow onset (5-8 minutes) and long duration of action[3] and is most commonly used. In subarachnoid block numerous adjuvants like morphine, clonidine, midazolam, dexmedetomidine and fentanyl etc have been added with hyperbaric bupivacaine to increase the duration of sensory and motor block, to provide stable haemodynamics and prolonged postoperative analgesia for below umbilical surgeries. Intrathecal opioids are most commonly used as they are synergistic with LA.

It is common practice to mix adjuvant drugs with hyperbaric LA in the same syringe but that can alter the density of LA solution influencing spread of the drug in the cerebrospinal fluid (CSF).[4] Various factors that have been shown to influence the intrathecal spread of LA are temperature and pH of the drug, baricity and patient position after injection.[5] Studies have already shown that premixing adjuvants with hyperbaric bupivacaine might alter its spread in CSF.[6] Conversely, administering adjuvants sequentially in separate syringes may minimise the change in density and pH of both drugs, preventing any alteration in CSF spread.

The density of CSF at 37°C is 1.00059g/ml.[7] Baricity of fentanyl is 0.99410 while that of hyperbaric bupivacaine is 1.02360. After addition of fentanyl in the same syringe as LA, baricity of the solution comes out to be 1.01850.[8] Alterations in the baricity of a solution to the extent of 0.0006 can alter the spread of LA in CSF.[9] Thus the addition of fentanyl to LA may alter the density of the mixture and affect the spread of LA hence affect the block characteristics.

Thus we undertook this study to evaluate the differences in block characteristics, mainly onset of block and duration of block along with determining effects on haemodynamics and postoperative pain relief in the patients undergoing below umbilical surgeries whilst administering hyperbaric bupivacaine and fentanyl as a mixture in a single syringe or sequentially in two separate syringes.

METHODS

After obtaining institutional ethical committee's approval and written informed consent of the patients, the present study was conducted on ninety patients of ASA grade I and II, aged between 18 and 60 years of either sex, who were undergone below umbilical elective surgeries. All the patients were considered otherwise healthy and not have any other medical treatment. Patients were randomly allocated by sealed envelope method into three equal groups of 30 patients each. Group A patients received premixed 2.5ml (12.5 mg) of heavy bupivacaine 0.5% and 0.5 ml (25 microgram) of fentanyl in a single 5.0 ml syringe. Group B patients received 0.5 ml (25 microgram) of fentanyl in a 2.0 ml syringe followed by 2.5 ml (12.5 mg) of heavy bupivacaine 0.5% in a 5.0 ml syringe and Group C patients received 2.5 ml (12.5 mg) of heavy bupivacaine 0.5% in a 5.0 ml syringe followed by 0.5 ml (25 microgram) of fentanyl in a 2.0 ml syringe.

Patients known or suspected to have any kind of allergy or having cardio-respiratory, metabolic, endocrinal, hepatic and renal disorder or any local pathology at the site of injury were excluded from the study. Pre-operatively patients were asked to keep nil by mouth for 6 hours. After intravenous insertion of an 18-G cannula in the operating room, all patients were preloaded with Ringer's lactate 15 ml/kg over 10 mins. All the routine monitors were attached, and the preoperative baseline readings of noninvasive blood pressure, pulse rate (PR), and saturation were noted. For the subarachnoid block, the patients were placed in the sitting position and after adequate aseptic precautions lumbar puncture was performed at L3–4 intervertebral space using a standard midline approach with a 25-G Quincke needle. After ensuring a free flow of CSF, the drug doses were injected intrathecally according to group allocated. The patients were placed in supine position immediately after spinal injection. The anaesthesiologists other than who performed the block recorded the intra operative data, and a nurse in post anaesthesia care unit (PACU) who followed the patients postoperatively until discharged from the PACU. Both were unaware of the group to which patient was allotted.

Sensory blockade was assessed by loss of sensation to pinprick method using 23 G hypodermic needle, bilaterally in the midclavicular line. Time of onset of sensory blockade was defined as completion of intrathecal injection to the loss of pinprick sensation at umbilical level (T-10 dermatome). Highest level of sensory block and time taken to achieve highest level of sensory block were noted. Duration of sensory block was defined as a time of onset of sensory block to sensory

regression to S- 2 dermatome. Degree of motor blockade was determined according to Modified Bromage Scale. Onset of motor block was defined as a time from intrathecal injection till the patient is unable to flex ankle and foot (Modified Bromage Score 3). Duration of motor block recorded and was considered as time from onset of motor block to recovery of Modified Bromage Score 0 (Table 1).

Intraoperatively, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), pulse rate (PR), oxygen saturation (SpO2) were recorded. Hypotension, defined as fall of MAP by >20% from baseline or fall of SBP below 90 mmHg, was treated with rapid infusion of i.v. fluids and incremental intravenous doses of mephentermine 6 mg. Bradycardia, defined as PR <50 bpm (beats per minute) or a decrease by >20% from baseline, was treated with injection atropine 0.6 mg intravenously. Respiration was monitored and respiratory depression was defined as respiratory rate <10 breath/min or Spo2 <92%, at that time oxygen was supplemented through mask at 5L/min.

All patients were observed for postoperative analgesia. Pain intensity was measured using a 10 cm Visual Analogue Scale (VAS) on 0 to 10 points (0 = no pain and 10 = worst pain). VAS score < 3 will be considered as effective analgesia. When VAS score reaches >3, injection diclofenac (75 mg) intravenously was given as rescue analgesic. Duration of effective analgesia was measured as the time from intrathecal injection to the first administration of rescue analgesic. Time for the first request for postoperative analgesia and the number of patients who required supplemental analgesic, were recorded. All patients were observed postoperatively for any complain of pruritus, nausea, vomiting, hypotension, bradycardia, respiratory depression, and post-spinal shivering. Intra and postoperative complications were noted and managed accordingly

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All the data were reported as mean±S.D. and results were subjected to statistical analysis using Student t-test and Chi square test. P-value <0.05 was considered statistically significant.

RESULTS

All patients were comparable with regards to demographic data (Table 2). The onset of pinprick analgesia at T10, the time for maximum extent of cephelad spread were significantly more rapid with group C then group B and after that group A. There was significant difference among the group with regard to the maximum block height achieved. The maximum block height achieved was significantly high in sequential groups B & C as compared to premixed group A. The onset time of motor block was significantly rapid in group C as compared to group A and group B. The total duration of motor block was significantly longer in sequential groups B & C as compared to premixed group A (Table 3).

There were significant differences among the groups with regard to the total duration of analgesia. The total duration of analgesia was significantly longer in sequential groups B & C as compared to premixed group A (Table 3). Total rescue analgesic requirement in post operative period was significantly more in premixed group A than sequential groups B & C (Table 3). Heart rate was decreased after spinal block in all groups but this fall in heart rate was statistically insignificant as compared to basal value at all time intervals in all three groups (Figure 1). There was significant difference in fall in mean arterial pressure in premixed group A as compared to sequential groups B & C (Figure 2). Patients were remained haemodynamically more stable in sequential groups i. e. group B & C as compared to premixed group A. Patients in group A experienced more nausea and vomiting due to more incidence of hypotension. However, incidence of side effects were comparable in all three groups.

DISCUSSION

Subarachnoid block is an old age technique which is relatively simple and advantageous as compared to general anaesthesia for below umbilical surgeries. Various additives administered concomitantly with local anaesthetic agent (LA) are fentanyl,[10] morphine,[11] clonidine,[12] dexmedetomidine,[13] and many more and have shown to improve the quality of block and postoperative analgesia with varying degree of success.

In the present study, an attempt was made to evaluate the differences in block characteristics, mainly onset of block and duration of block along with determining effects on haemodynamics and postoperative pain relief in the patients undergoing below umbilical surgeries whilst administering hyperbaric bupivacaine and fentanyl as a mixture in a single syringe or sequentially in two separate syringes.

In present study, patients in group C had significantly early onset time of sensory and motor block as compared to group A & B. Malhotra A. et al [1] and Bansal N. et al[14] also observed similar early onset time of sensory and motor block. The mean time to reach highest sensory block level was significantly less in group C as compared to group A & B. Our findings were in accordance with study results of Malhotra A. et al[1] and Desai S. et al.[15] Similar to results of Desai S. et al,[15] in our study time to two segment sensory regression was statistically significant in between group A & B and group A & C. However, group B & C were statistically comparable with regard to time to 2 segment regression of sensory block. Duration of sensory and motor block and duration of analgesia was significantly longer in group B & C as compared to group A. Other authors also reported similar results.[1,14,15,17,18] This difference might be due to the fact that fentanyl and bupivacaine as a mixture dilutes the potency of fentanyl and receptor occupancy might decrease leading to less pronounced effect. On the other hand, if fentanyl is administered separately a greater spread and thereby formation of stronger bonds with the opioid receptor in the spinal cord leads to denser and prolonged block.

In present study changes in heart rate were comparable in all three groups at all time intervals**.** After spinal anaesthesia block (SAB), mean arterial pressure (MAP) was decreased in all three groups at different time intervals. This decreased in MAP was statistically insignificant as compared to basal MAP in group B & C. However, in group A the fall in MAP was significant as compared to basal MAP at 5 min after SAB and it remained significantly low throughout the study period in comparison to basal value. However, group B & C were comparable with regard to changes in mean arterial pressure at different time intervals. In spite of fall in MAP, 8 patients out of 30 in group A and 1 patient out of 30 in group C received vasopressor due to fall in MAP >20% of baseline value. In group B hypotension was not reported. That suggests that although sequential administration of bupivacaine and fentanyl causes fall in MAP and set the MAP at lower normal limit but that does not make patient haemodynamically unstable. The results of our study correlates with that of study conducted by Malhotra A. et al,[1] Bansal N. et al[14] and Keera AAI et al.[16] In our opinion, hyperbaric bupivacaine injected separately being less dense, sinks down more as compared to lesser dense mixture of bupivacaine and fentanyl, and takes a longer time to reach final level. This delays the onset of sympathetic block and gives time for compensatory mechanisms of body to prevent hypotension.

Total doses of rescue analgesic used in group A was significantly more than group B & C. However, total rescue analgesic requirement was comparable in group B & C. In accordance with our study Malhotra A. et al[1] also observed similar result for total rescue analgesic requirement in postoperative period while comparing premixed and sequential administration of local anaesthetic agent and opioids during SAB.

We observed that patients in group A experienced more nausea and vomiting which might be due to more incidence of hypotension which lead to less cerebral blood flow and activation of vomiting center in medulla oblongata. However, incidence of side effects were comparable in all three groups.

We concluded that administering hyperbaric bupivacaine followed by fentanyl leads to an early onset and prolonged duration of sensory and motor block. Time to first requirement of analgesic (duration of analgesia) in postoperative period was longer when hyperbaric bupivacaine and fentanyl were given in sequential manner. However, as sample size was low, we recommened further studies to establish our findings.

Table 1: Modified Bromage Scale

Grade	Parameter
0	No motor block
1	Unable to raise extended legs
2	Unable to flex knee
3	Unable to flex ankle and foot

Table 2: Demographic characteristics

Variable	Group A	Group B	Group C
Age (years)	37.8±11.3	36.2±8.2	35.2±8.8

Sex (Male/Female)	15/15	16/14	16/14
Weight (kg)	65.9±6.7	68.2±6.0	68.2±6.0
ASA grade (1/2)	21/9	20/10	21/9
Duration of surgery (minutes)	84.5±6.2	84.0±6.2	84.1±5.9

Data: Mean ± SD or n.

Table 3: Sensory and motor characteristics comparison between group A, group B and group C

Characteristics	Group A	Group B	P value	Group A	Group C	P value	Group B	Group C	P value
Onset time of sensory block (min)	4.7±0.5	3.8±0.6	<0.0001	4.7±0.5	2.7±0.5	<0.0001	3.8±0.6	2.7±0.5	<0.0001
Onset time of motor block (min)	7.1±0.4	5.7±0.7	<0.0001	7.1±0.4	4.4±0.6	<0.0001	5.7±0.7	4.4±0.6	<0.0001
Time to reach highest sensory level (min)	8.4±0.6	6.9±0.5	<0.0001	8.4±0.6	5.8±0.6	<0.0001	6.9±0.5	5.8±0.6	<0.0001
Time to 2 segment regression of sensory block (min)	101.4±4.2	113.2±3.1	<0.0001	101.4±4.2	112.8±3.1	<0.0001	113.2±3.1	112.8±3.1	0.6191
Duration of motor block (min)	178.7±7.1	204.2±5.1	<0.0001	178.7±7.1	206.9±7.6	<0.0001	204.2±5.1	206.9±7.6	0.1116
Duration of sensory block (min)	194.3±8.3	218.8±1.9	<0.0001	194.3±8.3	220.1±4.2	<0.0001	218.8±1.9	220.1±4.2	0.1279
Duration of analgesia (min)	209.7±9.9	235.5±3.2	<0.0001	209.7±9.9	236.5±4.2	<0.0001	235.5±3.2	236.5±4.2	0.3039

Data: Mean ± SD

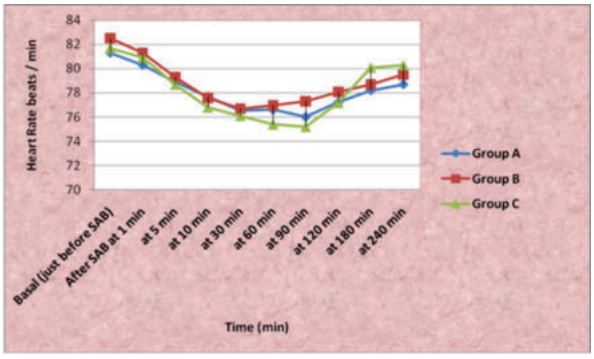

Fig 1: Changes in heart rate (beats per minute)

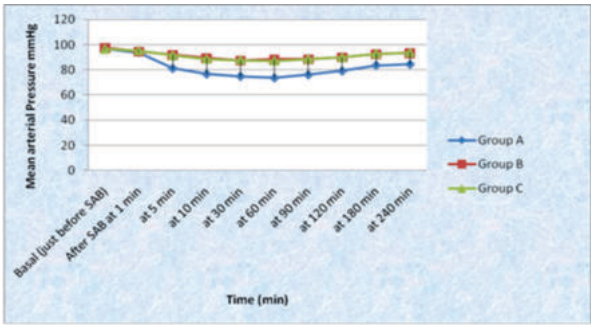

Fig 2: Changes in MAP

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